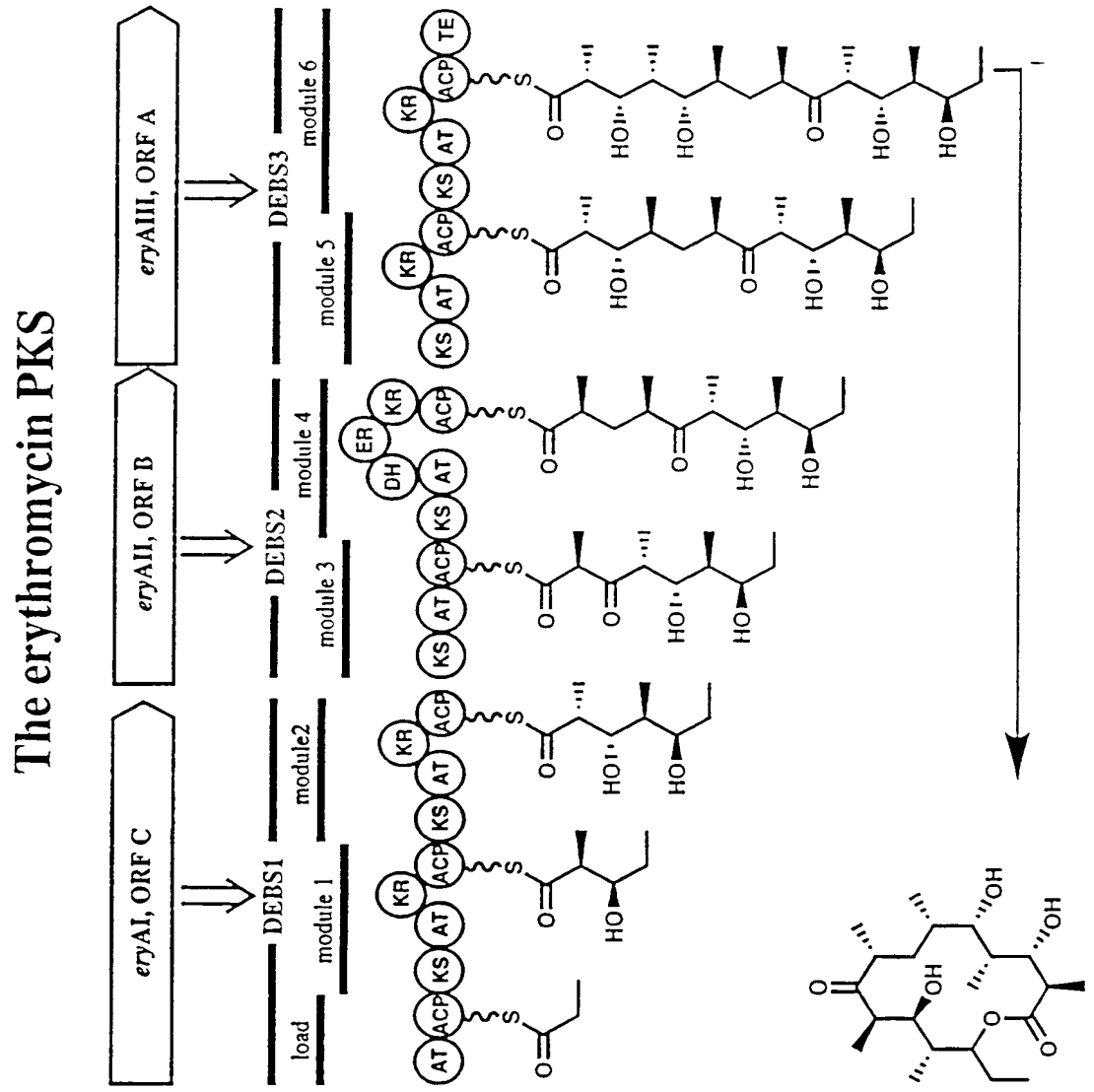

The erythromycin PKS
eryAI, ORF C
eryAII, ORF B
eryAIII, ORF A
DEBS1
DEBS2
DEBS3
load
module 1
module2
module 3
module 4
module 5
module 6
AT
ACP
KS
KR
DH
ER
TE
HO
OH
O

Fig. 1

```
KCLFDAU         ----------------------------MVTGLGIVAPNGLGVGAIWDAVLNGRNGIGPLR
KCLFPEU         MTGTAARTASSQLHASPAGRRGLRGRAVVTGLGIVAPNGLGVGAYWDAVLNGRNGIGPLR
KCLFACT         -------------------------MSVLITGVGVVAPNGLGLAPYWSAVLDGRHGLGPVT
KCLFHIR         -------------------------MSTWVTGMGVVAPNGLGADDHWAATLKGRHGISRLS
KCLFGRA         -------------------MSTPDRRRAVVTGLSVAAPGGLGTERYWKSLLTGENGIAELS
KCLFNOG         ----------------------MTAAVVVTGLGVVAPTGLGVREHWSSTVRGASAIGPVT
KCLFTCM         --------------------MSAPAPVVVTGLGIVAPNGTGTEEYWAATLAGKSGIDVIQ
KCLFCIN         ----------------------MTP-VAVTGMGIAAPNGLGRPTTGRPPWAPRAASAAST
KCLFVNZ         ----------------------MSASVVVTGLGVAAPNGLGREDFWASTLGGKSGIGPLT
KCLFWHIE        -----------MSGPQRTGTGGGSRRAVVTGLGVLSPHGTGVEAHWKAVADGTSSLGPVT
KSGRA           ----------------------MTRRVVITGVGVRAPGGSGTKEFWDLLTAGRTATRPIS
KSHIR           ----------------------MTRRVVITGVGVRAPGGLGAKNFWELLTSGRTATRRIS
KSACT           ----------------------MKRRVVITGVGVRAPGGNGTRQFWELLTSGRTATRRIS
KSCIN           ---------------------MTQRRVAITGIEVLAPGGLGRKEFWQLLSEGRTATRGIT
KSVNZ           ---------------------MTARRVVITGIEVLAPGGTGSKAFWNLLSEGRTATRGIT
KSNOG           -------------------MKESINRRVVITGIGIVAPDATGVKPFWDLLTAGRTATRTIT
KSTCM           -------------------MTRHAEKRVVITGIGVRAPGGAGTAAFWDLLTAGRTATRTIS
KSDAU           ----------------------MNRRVVITGMGVVAPGAIGIKSFWELLLSGTTATRAIT
KSPEU           ----------------------MNRRIVITGIGVVAPGAVGTKPFWELLLSGTTATRAIS
KSWHI           ----------------------MTRRRVAVTGIGVVAPGGIGTPQFWRLLSEGRTATRRIS
                                       :**: : :* . *                .

KCLFDAU         RFADDGRLGRLAGEVSDFVP-EDHLPKRLLVQTDPMTQMTALAAAEWALREAGCAPSS--
KCLFPEU         RFTGDGRLGRLAGEVSDFVP-EDHLPKRLLAQTDPMTQY-ALAAAEWALRESGCSPSS--
KCLFACT         RFDVSRYPATLAGQIDDFHA-PDHIPGRLLPQTDPSTRL-ALTAADWALQDAKADPES-L
KCLFHIR         RFDPTGYPAELAGQVLDFDA-TEHLPKRLLPQTDVSTRF-ALAAAAWALADAEVDPAE-L
KCLFGRA         RFDASRYPSRLAGQIDDFEA-SEHLPSRLLPQTDVSTRY-ALAAADWALADAGVGPESGL
KCLFNOG         RFDAGRYPSKLAGEVPGFVP-EDHLPSRLMPQTDHMTRL-ALVAADWAFQDAAVDPSK-L
KCLFTCM         RFDPHGYPVRVGGEVLAFDA-AAHLPGRLLPQTDRMTQH-ALVAAEWALADAGLEPEK-Q
KCLFCIN         RFDPSGYPAQLAGEIPGFRA-AEHLPGRLVPQTDRVTRL-SLAAADWALADAGVEVAA-F
KCLFVNZ         RFDPTGYPARLAGEVPGFAA-EEHLPSRLLPQTDRMTRL-ALVAADWALADAGVRPEE-Q
KCLFWHIE        REGCAHLPLRVAGEVHGFDA-AETVEDRFLVQTDRFTHF-ALSATQHALADARFGRADVD
KSGRA           FFDASPFRSRIAGEI-DFDAVAEGFSPREVRRMDRATQF-AVACTRDALADSGLDTGA-L
KSHIR           FFDPTPNRSQIAAEC-DFDPEHEGLSPREIRRMDRAAQF-AVVCTRDAVADSGLEFEQ-V
KSACT           FFDPSPYRSQVAAEA-DFDPVAEGFGPRELDRMDRASQF-AVACAREAFAASGLDPDT-L
KSCIN           FFDPAPFRSKVAAEA-DFCGLENGLSPQEVRRMDRAAQF-AVVTAR-AVEDSGAELAA-H
KSVNZ           FFDPTPFRSRVAAEI-DFDPEAHGLSPQEIRRMDRAAQF-AVVAAR-AVADSGIDLAA-H
KSNOG           AFDPSPFRSRIAAEC-DFDPLAEGLTPQQIRRMDRATQF-AVVSARESLEDSGLDLGA-L
KSTCM           LFDAAPYRSRIAGEI-DFDPIGEGLSPRQASTYDRATQL-AVVCAREALKDSGLDPAA-V
KSDAU           TFDATPFRSRIAAEC-DFDPVAAGLSAEQARRLDRAGQF-ALVAGQEALTDSGLRIGE-D
KSPEU           TFDATPFRSRIAAEC-DFDPVAAGLSAEQARRLDRAGQF-ALVAGQEALADSGLRIDE-D
KSWHI           LFDPSGLRSQIAAEC-DFEPSDHGLGLATAQRCDRYVQF-ALVAASEAVRDANLDMNR-E
                          :..:   *      .        *   :  ::     :.  :
```

Fig 2A

```
KCLFDAU    -PLEAGVITASASGGFASGQRELQNLWSKG-----PAHVSAYMSFAWFY-AVNTGQIAIR
KCLFPEU    -PLEAGVITASASGGFAFGQRELQNLWSKG-----PAHVSAYMSFAWFY-AVNTGQIAIR
KCLFACT    TDYDMGVVTANACGGFDFTHREFRKLWSEG-----PKSVSVYESFAWFY-AVNTGQISIR
KCLFHIR    PEYGTGVITSNATGGFEFTHREFRKLWAQG-----PEFVSVYESFAWFY-AVNTGQISIR
KCLFGRA    DDYDLGVVTSTAQGGFDFTHREFHKLWSQG-----PAYVSVYESFAWFY-AVNTGQISIR
KCLFNOG    PEYGVGVVTASSAGGFEFGHRELQNLWSLG-----PQYVSAYQSFAWFY-AVNTGQVSIR
KCLFTCM    DEYGLGVLTAAGAGGFEFGQREMQKLWGTG-----PERVSAYQSFAWFY-AVNTGQISIR
KCLFCIN    DPLDMGVVTASHAGGFEFGQDELQKLLGQG-----QPVLSAYQSFAWFY-AVNSGQISIR
KCLFVNZ    DDFDMGVVTASASGGFEFGQGELQKLWSQG-----SQYVSAYQSFAWFY-AVNSGQISIR
KCLFWHIE   SPYSVGVVTAAGSGGGEFGQRELQNLWGHG-----SRHVGPYQSIAWFY-AASTGQVSIR
KSGRA      DPSRIGVALGSAVASATSLENEYLVMSDSGREWLVDPAHLSPMMFDYLSPGVMPAEVAWA
KSHIR      PPERIGVSLGSAVAAATSLEQEYLVLSDGGREWQVDPAYLSAHMFDYLSPGVMPAEVAWT
KSACT      DPARVGVSLGSAVAAATSLEREYLLLSDSGRDWEVDAAWLSRHMFDYLVPSVMPAEVAWA
KSCIN      PPHRIGVVVGSAVGATMGLDNEYRVVSDGGRLDLVDHRYAVPHLYNYLVPSSFAAEVAWA
KSVNZ      DPYRVGVTVGSAVGATMGLDEEYRVVSDGGRLDLVDHAYAVPHLYDYMVPSSFSAEVAWA
KSNOG      DASRTGVVVGSAVGCTTSLEEEYAVVSDSGRNWLVDDGYAVPHLFDYFVPSSIAAEVAHD
KSTCM      NPERIGVSIGTAVGCTTGLDREYARVSEGGSRWLVDHTLAVEQLFDYFVPTSICREVAWE
KSDAU      SAHRVGVCVGTAVGCTQKLESEYVALSAGGANWVVDPHRGAPELYDYFVPSSLAAEVAWL
KSPEU      SAHRVGVCVGTAVGCTQKLESEYVALSAGGAHWVVDPGRGSPELYDYFVPSSLAAEVAWL
KSWHI      DPWRAGATLGTAVGGTTRLEHDYVLVSERGSRWDVDDRRSEPHLERAFTPATLSSAVAEE
                  *.  .   .   . :   :  *                 :         ::

KCLFDAU    -HDLRGPVGVVVAEQAGGLDALAHAR-RKVRGGAE-LIVSGAMDSSLCP-YGMAAQVRSG
KCLFPEU    -HDLRGPVGVVVAEQAGGLDALAHAR-RKVRGGAE-LIVSGAVDSSLCP-YGMAAQVKSG
KCLFACT    -HGMRGPSSALVAEQAGGLDALGHAR-RTIRRGTP-LVVSGGVDSALDP-WGWVSQIASG
KCLFHIR    -HGLRGPGSVLVAEQAGGLDAVGHGG--AVRNGTP-MVVTGGVDSSFDP-WGWVSHVSSG
KCLFGRA    -NTMRGPSAALVGEQAGGLDAIGHAR-RTVRRGPG-WCSAVASTRRSTR-GASSSQLSGG
KCLFNOG    -HGLRGPGGVLVTEQAGGLDALGQAR-RQLRRGLP-MVVAGAVDGSPCP-WGWVAQLSSG
KCLFTCM    -HGMRGHSSVFVTEQAGGLDAAAHAA-RLLRKGTLNTALTGGCEASLCP-WGLVAQIPSG
KCLFCIN    -HGMKGPSGVVVSDQAGGLDALAQAR-RLVRKGTP-LIVCGAVEPRSAPGAGSPSSPAGG
KCLFVNZ    -NGMKGPSGVVVSDQAGGLDAVAQAR-RQIRKGTR-LIVSGGVDASLCP-WGWVAHVASD
KCLFWHIE   -NDFKGPCGVVAADEAGGLDALAHAA-LAVRNGTD-TVVCGATEAPLAP-YSIVCQLGYP
KSGRA      -AGAEGPVTMVSDGCTSGLDSVGYAV-QGTREGSADVVVAGAADTPVSPIVVACFDAIKA
KSHIR      -VGAEGPVAMVSDGCTSGLDSLSHAC-SLIAEGTTDVMVAGAADTPITPIVVSCFDAIKA
KSACT      -VGAEGPVTMVSTGCTSGLDSVGNAV-RAIEEGSADVMFAGAADTPITPIVVACFDAIRA
KSCIN      -VGAEGPSTVVSTGCTSGIDAVGIAV-ELVREGSVDVMVAGAVDAPISPIP-CVLDAIKA
KSVNZ      -VGAEGPNTVVSTGCTSGLDSVGYARGELIREGSADVMIAGSSDAPISPITMACFDAIKA
KSNOG      RIGAEGPVSLVSTGCTSGLDAVGRAA-DLIAEGAADVMLAGATEAPISPITVACFDAIKA
KSTCM      -AGAEGPVTVVSTGCTSGLDAVGYGT-ELIRDGRADVVVCGATDAPISPITVACFDAIKA
KSDAU      -AGAEGPVNIVSAGCTSGIDSIGYAC-ELIREGTVDVMLAGGVDAPIAPITVACFDAIRV
KSPEU      -AGAEGPVNIVSAGCTSGIDSIGYAC-ELIREGTVDAMVAGGVDAPIAPITVACFDAIRA
KSWHI      -FGVRGPVQTVSTGCTSGLDAVGYAY-HAVAEGRVDVCLAGAADSPISPITMACFDAIKA
            .*     .     . .*:*:  .  .         *          .

KCLFDAU    RLSGSDDPTAGYLPFDRRAAGHVPGEG-GAILAVEDAERVAERG-GKVYGSIAGT-ASFD
KCLFPEU    RLSGSDNPTAGYLPFDRRAAGHVPGEG-GAILTVEDAERAAERG-AKVYGSIAGYGASFD
KCLFACT    RISTATDPDRAYLPFDERAAGYVPGEG-GAILVLEDSAAAEARGRHDAYGELAGCASTFD
KCLFHIR    RVSRATDPGRAYLPFDVAANGYVPGEG-GAILLLEDAESAKARG-ATGYGEIAGYAATFD
KCLFGRA    LVSTVADPERAYLPFDVDASGYVPGEG-GAVLIVEDADSARARG---AERIYVRSPLRRD
KCLFNOG    GLSTSDDPRRAYLPFDAAAGGHVPGEG-GALLVLESDESARARGVTRWYGRIDGYAATFD
KCLFTCM    FLSEATDPHDAYLPFDARAAGYVPGEG-GAMLVAERADSARERDAATVYGRIAGHASTFD
KCLFCIN    -MSDSDEPNRAYLPFDRDGRGYVPGGGRGVVPPLERAEAAPARG-AEVYGE-AGPLARL-
KCLFVNZ    RLSTSEEPARGYLPFDREAQGHVPGEG-GAILVMEAAEAARERG-ARIYGEIAGYGSTFD
KCLFWHIE   ELSRATEPDRAYRPFTEAACGFAPAEG-GAVLVVEEEAAARERG-ADVRATVAGHAATFT
```

Fig 2B

```
KSGRA       TTPRNDDPAHASRPFDGTRNGFVLAEG-AAMFVLEEYEAAQRRG-AHIYAEVGGYATRSQ
KSHIR       TTPRNDDPEHASRPFDNSRNGFVLAEG-AALFVLEELEHARARG-AHVYAEISGCATRLN
KSACT       TTARNDDPEHASRPFDGTRDGFVLAEG-AAMFVLEDYDSALARG-ARIHAEISGYATRCN
KSCIN       TTPRHDAPATASRPFDSTRNGFVLGEG-AAFFVLEELHSARRRG-AHIYAEIAGYATRSN
KSVNZ       TTNRYDDPAHASRPFDGTRNGFVLGEG-AAVFVLEELESARARG-AHIYAEIAGYATRSN
KSNOG       TTPRNDTPAEASRPFDRTRNGFVLGEG-AAVFVLEEFEHARRRG-ALVYAEIAGFATRCN
KSTCM       TSANNDDPAHASRPFDRNRDGFVLGEG-SAVFVLEELSAARRRG-AHAYAEVRGFATRSN
KSDAU       TSDHNDTPETLA-PFSRSRNGFVLGEG-GAIVVLEEAEAAVRRG-ARIYAEIGGYASRGN
KSPEU       TSDHNDTPETASRPFSRSRNGFVLGEG-GAIVVLEEAEAAVRRG-ARIYAEIGGYASRGN
KSWHI       TSPNNDDPAHASRPFDADRNGFVMGEG-AAVLVLEDLEHARARG-ADVYCEVSGYATFGN
                      *     **      *.. . * ...   *     .  *.

KCLFDAU     -PPPGSGRP---SALARAVETALADAGLDRSDIAVVFADGAA-VGELDVAEAEALASVFG
KCLFPEU     -PPPGSGRP---SALARAVETALADAGLDGSDIAVVFADGAA-VPELDAAEAEALASVFG
KCLFACT     -PAPGSGRP---AGLERAIRLALNDAGTGPEDVDVVFADGAG-VPELDAAEARAIGRVFG
KCLFHIR     -PAPGSERP---PALRRAIELALADAELRPEQVDVVFADAAG-VAELDAIEAAAIRELFG
KCLFGRA     -PAPGSGRP---PALGRAAELALAEAGLTPADISVVFADGAG-VPELDRAEADTLARLFG
KCLFNOG     -PPPGSGRP---PNLLRAAQAALDDAEVGPEAVDVVFADASG-TPDEDAAEADAVRRLFG
KCLFTCM     -ARPGTGRP---TGPARAIRLALEEARVAPEDVDVVYADAAG-VPALDRAEAEALAEVFG
KCLFCIN     -PAPHSGRG---STRAHAIRTALDDAGTAPGDIRRVFADGGGRYPN-DRAEAEAISEVFG
KCLFVNZ     -PRPGSGRE---PGLRKAIELALADAGAAPGDIDVVFADAAA-VPELDRVEAEALNAVFG
KCLFWHIE    GAGRWAESR---EGLARAIQGALAEAGCRPEEVDVVFADALG-VPEADRAEALALADALG
KSGRA       -AYHMTGLKKDGREMAESIRAALDEARLDRTAVDYVNAHGSG-TKQNDRHETAAFKRSLG
KSHIR       -AYHMTGLKTDGREMAEAIRVALDLARIDPTDIDYINAHGSG-TKQNDRHETAAFKRSLG
KSACT       -AYHMTGLKADGREMAETIRVALDESRTDATDIDYINAHGSG-TRQNDRHETAAYKRALG
KSCIN       -AYHMTGLR-DGAEMAEAIRLALDEARLNPEQVDYINAHGSG-TKQNDRHETAAFKKALG
KSVNZ       -AYHMTGLRPDGAEMAEAIRVALDEARMNPTEIDYINAHGSG-TKQNDRHETAAFKKSLG
KSNOG       -AFHMTGLRPDGREMAEAIGVALAQAGKAPADVDYVNAHGSG-TRQNDRHETAAFKRSLG
KSTCM       -AFHMTGLKPDGREMAEAITAALDQARRTGDDLHYINAHGSG-TRQNDRHETAAFKRSLG
KSDAU       -AYHMTGLRADGAEMAAAITAALDEARRDPSDVDYVNAHGTA-TRQNDRHETSAFKRSLG
KSPEU       -AYHMTGLRADGAEMAAAITAALDEARRDPSDVDYVNAHGTA-TKQNDRHETSAFKRSLG
KSWHI       -AYHMTGLTKEGLEMARAIDTALDMAELDGSAIDYVNAHGSG-TQQNDRHETAAVKRSLG
             .   :          :   **  :      :  : *.. .     *  *: :    :*
```

Fig 2c

```
KCLFDAU         P--HRVPVTVPKTLTGRLYSGAGPLDVATGLLALRDEVVPATGHVH-PDPDLPLDVVTGR
KCLFPEU         P--RRVPVTVPKTLTGRLYSGAGPLDVATALLALRDEVVPATAHVD-PDPDLPLDVVTGR
KCLFACT         R--EGVPVTVPKTTTGRLYSGGGPLDVVTALMSLREGVIAPTAGVTSVPREYGIDLVLGE
KCLFHIR          P--SGVPVTAPKTMTGRLYSGGGPLDLVAALLAIRDGVIPPTVHTAEPVPEHQLDLVTGD
KCLFGRA          P--RGVPVTAPKALTGRLCAGGGPADLAAALLALRDQVIPATGRHRAVPDAYALDLVTGR
KCLFNOG          P--YGVPVTAPKTMTGRLSAGGAALDVATALLALREGVVPPTVNVSRPRPEYELDLVLA-
KCLFTCM          P--GAVPVTAPKTMTGRLYAGGAALDVATALLSIRDCVVPPTVGTGAPAPGLGIDLVLHQ
KCLFCIN          P--GRVPVTCPRTMTGRLHSGAAPLDVACALLAMRAGVIPPTVHID-PCPEYDLDLVLYQ
KCLFVNZ          T--GAVPVTAPKTMTGRLYSGAAPLDLAAAFLAMDEGVIPPTVNVE-PDAAYGLDLVVGG
KCLFWHIE         PHAARVPVTAPKTGTGRAYCAAPVLDVATAVLAMEHGLIPPTPHVL--DVCHDLDLVTGR
KSGRA            EHAYAVPVSSIKSMGGHSLGAIGSIEIAASVLAIEHNVVPPTANLHTPDPECDLDYVPLT
KSHIR            EHAYRTPVSSIKSMVGHSLGAIGSIEVAACALAIEHGVVPPTANLHEPDPECDLDYVPLT
KSACT            EHARRTPVSSIKSMVGHSLGAIGSLEIAACVLALEHGVVPPTANLRTSDPECDLDYVPLE
KSCIN            EHAYRTPVSSIKSMVGHSLGAIGSIEIAASALAMEYDVVPPTANLHTPDPECDLDYVPLT
KSVNZ            DHAYRTPVSSIKSMVGHSLGAIGSIEIAASALAMEHNVVPPTGNLHTPDPECDLDYVR-S
KSNOG            DHAYRVPVSSIKSMIGHSLGAIGSLEIAASVLAITHDVVPPTANLHEPDPECDLDYVPLR
KSTCM            QRAYDVPVSSIKSMIGHSLGAIGSLELAACALAIEHGVIPPTANYEEPDPECDLDYVPNV
KSDAU            DHAYRVPISSVKSMIGHSLGAAGSLEVAATALAVEYGAIPPTANLHDPDPELDLDYVPLT
KSPEU            EHAYRVPISSIKSMIGHSLGAVGSLEVAATALAVEYGVIPPTANLHDPDPELDLDYVPLT
KSWHI            EHAYATPMSSIKSMVGHSLGAIGSIELAACVLAMAHQVVPPTANYTTPDPECDLDYVPRE
                       .*::  ::  *:   .    ::.   :::    :..*           :* *

KCLFDAU          PRAMADARAALVVARGHGGFNSALVVRGAA-------
KCLFPEU          PRSLADARAALLVARGYGGFNSALVVRGAA-------
KCLFACT          PRSTAPRTA-LVLARGRWGFNSAAVLRRFAPTP----
KCLFHIR          PRHQQLGTA-LVLARGKWGFNSAVVVRGVTG------
KCLFGRA          PREAALSAA-LVLARGRHGFNSAVVVTLRGSDHRRPT
KCLFNOG          PRRTPLARA-LVLARGRGGFNAAMVVAGPRAETR---
KCLFTCM          PRELRVDTA-LVVARGMGGFNSALVVRRHG-------
KCLFCIN          VRPAALRTA-LGGARGHGGFNSALVVRAGQ-------
KCLFVNZ          PRTAEVNTA-LVIARGHGGFNSAMVVRSAN-------
KCLFWHIE         ARPAEPRTA-LVLARGLMGSNSALVLRRGAVPPEGR-
KSGRA            AREQRVDTV-LTVGSGFGGFQSAMVLHRPEEAA----
KSHIR            AREQRVDTV-LSVGSGFGGFQSAMVLRRLGGANS---
KSACT            ARERKLRSV-LTVGSGFGGFQSAMVLRDAETAGAAA-
KSCIN            ARDQRVDSV-LTVGSGFGGFQSAMVLTSAQ---RSTV
KSVNZ            CREQLTDSV-LTVGSGFGGFQSAMVLARPE---RKIA
KSNOG            ARACPVDTV-LTVGSGFGGFQSAMVLCGPGSRGRSAA
KSTCM            AREQRVDTV-LSVGSGFGGFQSAAVLARPKETRS---
KSDAU            AREKRVRHA-LTVGSGFGGFQSAMLLSRPER------
KSPEU            AREKRVRHA-LTVGSGFGGFQSAMLLSRLER------
KSWHI            ARERTLRHV-LSVGSGFGGFQSAVVLSGSEGGLR---
                  *       . *  . *  * ::* ::

mole:~/ks2%
```

Fig 2D

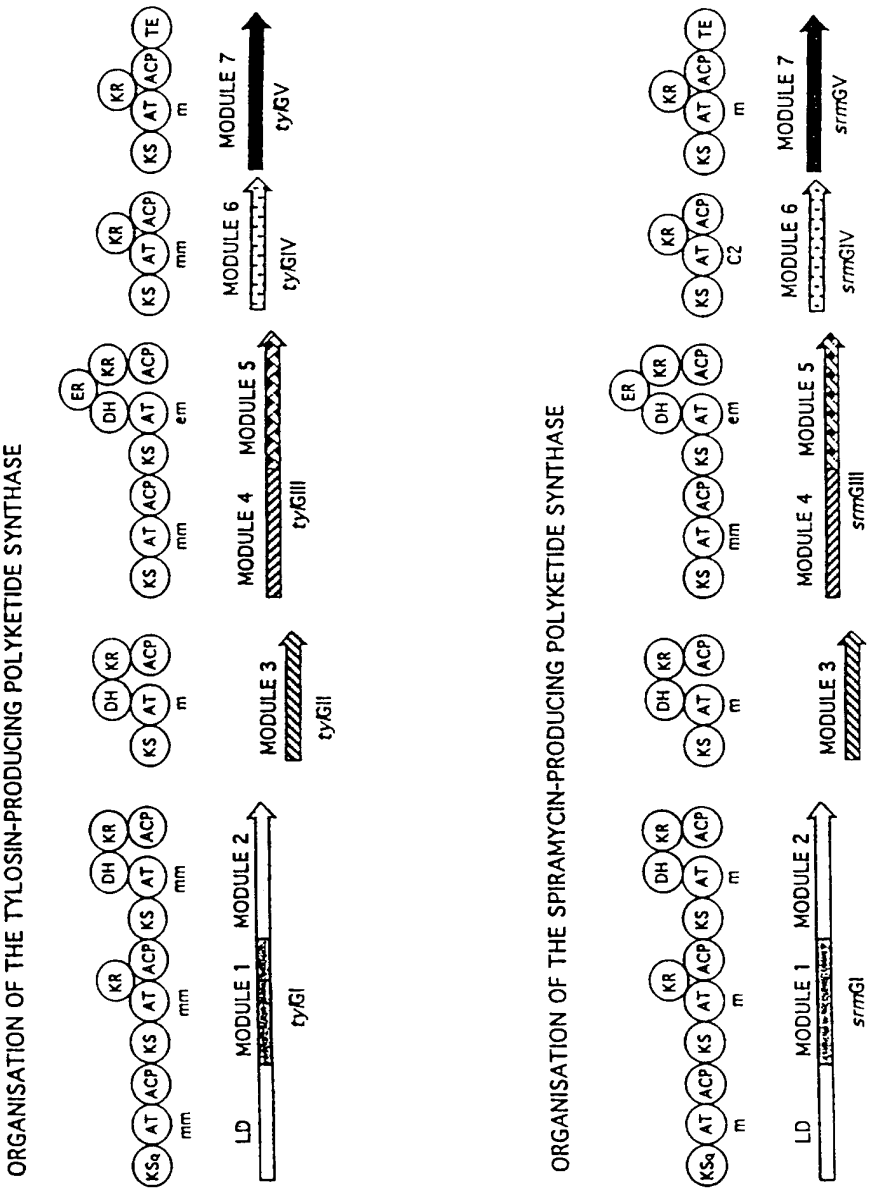

ORGANISATION OF THE TYLOSIN-PRODUCING POLYKETIDE SYNTHASE
LD
MODULE 1
MODULE 2
MODULE 3
MODULE 4
MODULE 5
MODULE 6
MODULE 7
tylGI
tylGII
tylGIII
tylGIV
tylGV
ORGANISATION OF THE SPIRAMYCIN-PRODUCING POLYKETIDE SYNTHASE
srmGI
srmGII
srmGIII
srmGIV
srmGV

Fig 3A

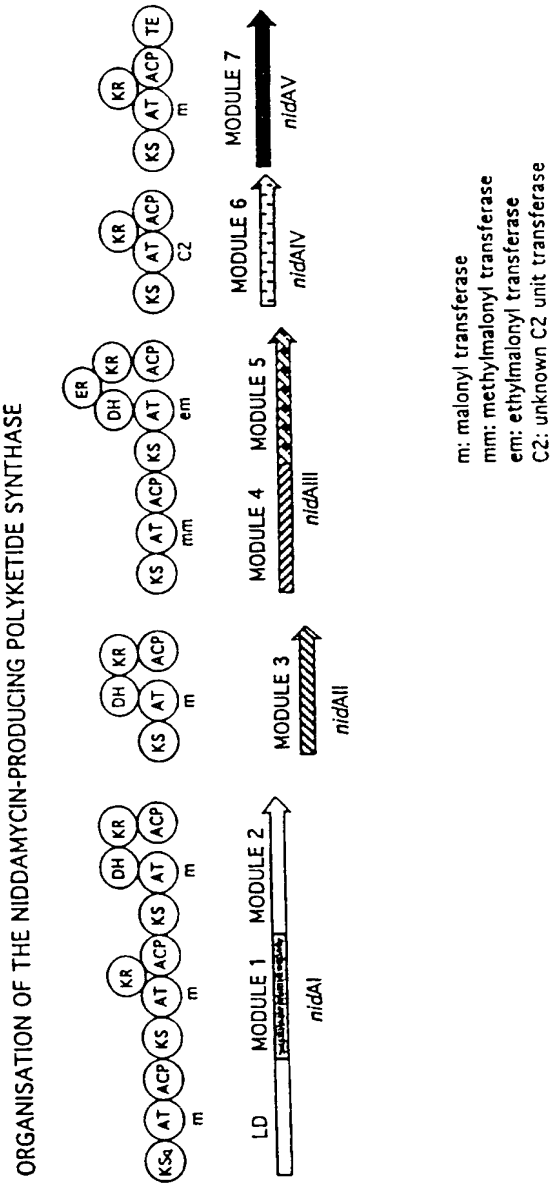

ORGANISATION OF THE NIDDAMYCIN-PRODUCING POLYKETIDE SYNTHASE
LD
MODULE 1
MODULE 2
MODULE 3
MODULE 4
MODULE 5
MODULE 6
MODULE 7
nidAI
nidAII
nidAIII
nidAIV
nidAV
m: malonyl transferase
mm: methylmalonyl transferase
em: ethylmalonyl transferase
C2: unknown C2 unit transferase

Fig 3B

```
                1                                                    50
niddamycin  ~~~~~~~~~ ~~~~~~~~~~ MAGHGDATAQ KAQDAEKSED GSDAIAVIGM
platenolide ~~~~~~~~~ ~~~~~~~~~~ ~~~~~~~~MS GELAISRSDD RSDAVAVVGM
monensin    ~~~~~~~~~ ~~~~~~~~~~ ~~~~~~MAAS ASASPSGPSA GPDPIAVVGM
oleandomycin~~~~~~~~~ ~~~~~~~~~~ ~~~~~~~~~~ ~~~MHVPGEE NGHSIAIVGI
tylosin     MSSALRRAVQ SNCGYGDLMT SNTAAQNTGD QEDVDGPDST HGGEIAVVGM

               51                                                   100
niddam...   SCRFPGAPGT AEFWQLLSSG ADAVVTAADG RRR..... .....GTIDA
platenol.   ACRFPGAPGI AEFWKLLTDG RDAIGRDADG RRR..... .....GMIEA
monensin    ACRLPGAPDP DAFWRLLSEG RSAVSTAPPE RRRADSGLHG P...GGYLDR
oleandom    ACRLPGSATP QEFWRLLADS ADALDEPPAG RFPTGSLSSP PAPRGGFLDS
tylosin     SCRLPGAAGV EEFWELLRSG RGMPTRQDDG TWRAA..... .......LED

              101                                                   150
niddam...   PADFDAAFFG MSPREAAATD PQQRLVLELG WEALEDAGIV PESLRGEAAS
platenol.   PGDFDAAFFG MSPREAAETD PQQRLMLELG WEALEDAGIV PGSLRGEAVG
monensin    IDGFDADFFH ISPREAVAMD PQQRLLLELS WEALEDAGIR PPTLARSRTG
oleandom    IDTFDADFFN ISPREAGVLD PQQRLALELG WEALEDAGIV PRHLRGTRTS
tylosin     HAGFDAGFFG MNARQAAATD PQHRLMLELG WEALEDAGIV PGDLTGTDTG

              151                                                   200
niddam...   VFVGAMNDDY ATLLH.RAGA PTDTYTATGL QHSMIANRLS YFLGLRGPSL
platenol.   VFVGAMHDDY ATLLH.RAGA PVGPHTATGL QRAMLANRLS YVLGTRGPSL
monensin    VFVGAFWDDY TDVLNLRAPG AVTRHTMTGV HRSILANRIS YAYHLAGPSL
oleandom    VFMGAMWDDY AHLAHARGEA ALTRHSLTGT HRGMIANRLS YALGLQGPSL
tylosin     VFAGVASDDY A.VLTRRSAV SAGGYTATGL HRALAANRLS HFLGLRGPSL

              201                                                   250
niddam...   VVDTGQSSSL VAVALAVESL RGGTSGIALA GGVNLVLAEE GS.AAMERVG
platenol.   AVDTAQSSSL VAVALAVESL RAGTSRVAVA GGVNLVLADE GT.AAMERLG
monensin    TVDTAQSSSL VAVHLACESI RSGDSDIAFA GGVNLICSPR TTELAAARFG
oleandom    TVDTGQSSSL AAVHMACESL ARGESDLALV GGVNLVLDPA GT.TGVERFG
tylosin     VVDSAQSASL VAVQLACESL RRGETSLAVA GGVNLILTEE ST.TVMERMG

              251                                                   300
niddam...   ALSPDGRCHT FDARANGYVR GEGGAIVVLK PLADALADGD RVYCVVRGVA
platenol.   ALSPDGRCHT FDARANGYVR GEGGAAVVLK PLADALADGD PVYCVVRGVA
monensin    GLSAAGRCHT FDARADGFVR GEGGGLVVLK PLAAARRDGD TVYCVIRGSA
oleandom    ALSPDGRCYT FDSRANGYAR GEGGVVVVLK PTHRALADGD TVYCEILGSA
tylosin     ALSPDGRCHT FDARANGYVR GEGGGAVVLK PLDAALADGD RVYCVIKGGA

              301                                                   350
niddam...   TGNDGGGPGL TVPDRAGQEA VLRAACDQAG VRPADVRFVE LHGTGTPAGD
platenol.   VGNDGGGPGL TAPDREGQEA VLRAACAQAR VDPAEVRFVE LHGTGTPVGD
monensin    VNSDGTTDGI TLPSGQAQQD VVRLACRRAR ITPDQVQYVE LHGTGTPVGD
oleandom    LNNDGATEGL TVPSARAQAD VLRQAWERAR VAPTDVQYVE LHGTGTPAGD
tylosin     VNNDGGGASL TTPDREAQEA VLRQAYRRAG VSTGAVRYVE LHGTGTRAGD
```

Fig 4A

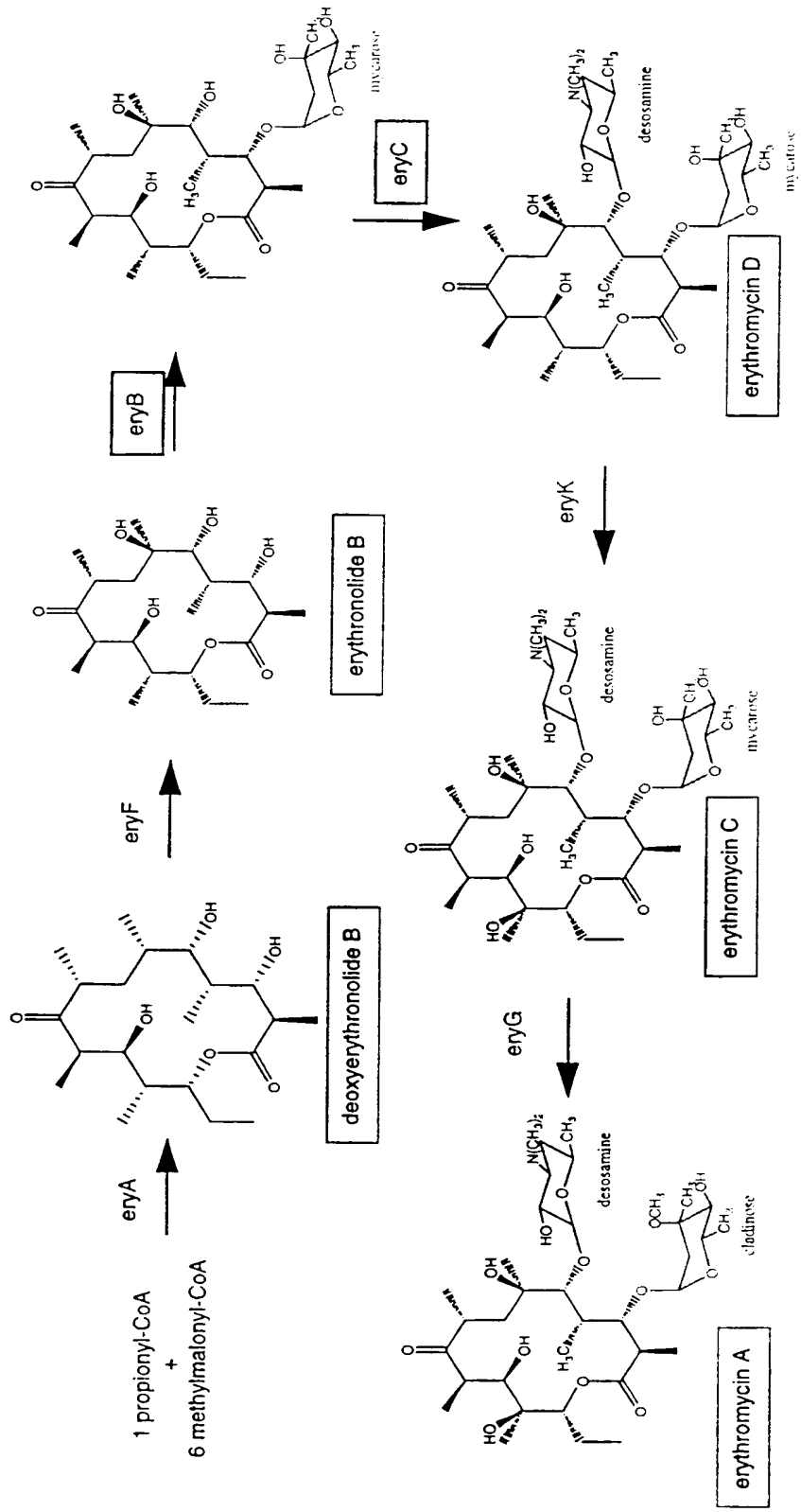
```
            351                                                        400
niddam...   PVEAEALGAV YGTGRP..AN EPLLVGSVKT NIGHLEGAAG IAGFVKAALC
platenol.   PVEAHALGAV HGSGRP..AD DPLLVGSVKT NIGHLEGAAG IAGLVKAALC
monensin    PIEAAALGAA LGQDAA..RA VPLAVGSAKT NVGHLEAAAG IVGLLKTALS
oleandom    PVEAEGLGTA LGTARP..AE APLLVGSVKT NIGHLEGAAG IAGLLKTVLS
tylosin     PVEAAALGAV LGAGADSGRS TPLAVGSVKT NVGHLEGAAG IVGLIKATLC

            401                                                        450
niddam...   LHERALPASL NFETPNPAIP LERLRLKVQT AHAALQPGTG GGPLLAGVSA
platenol.   LRERTLPGSL NFATPSPAIP LDQLRLKVQT AAAELPLAPG GAPLLAGVSS
monensin    IHHRRLAPSL NFTTPNPAIP LADLGLTVQQ DLADWP..RP EQPLIAGVSS
oleandom    IKNRHLPASL NFTSPNPRID LDALRLRVHT AYGPWP..SP DRPLVAGVSS
tylosin     VRKGELVPSL NFSTPNPDIP LDDLRLRVQT ERQEW.NEED DRPRVAGVSS

            451                                                        500
niddam...   FGMGGTNCHV VLEETPGG.. .......... .......... ...RQPAE.T
platenol.   FGIGGTNCHV VLEHLPSR.. .......... .......... ...PTPAV.S
monensin    FGMGGTNGHV VVA....AAP DSVAVPEPVG VPERVEVPEP VVVSEPVVVP
oleandom    FGMGGTNCHV VLSELRNAGG DGAGKGPYTG TEDRLGATEA EKRPDPATGN
tylosin     FGMGGTNVHL VIAEAPAAAG SSGAGGSGAG SGAGISAVSG VV........

            501                                                        550
niddam...   GQADACLFSA SPMLLLSARS EQALRAQAAR LREHL..EDS GADPLDIAYS
platenol.   VAAS...LPD VPPLLLSARS EGALRAQAVR LGETV..ERV GADPRDVAYS
monensin    TPWP...... .....VSAHS ASALRAQAGR LRTHLAAHRP TPDAARVGHA
oleandom    GPDPAQDTHR YPALILSARS DAALRAQAER LRHHL.EHSP GQRLRDTAYS
tylosin     .......... ..PVVVSGRS RVVVREAAGR LAE..VVEAG GVGLADVAVT

            551                                                        600
niddam...   LATTRTRFEH RAAVPCGDPD RLSSALAALA AGQTPRGVRI GS..TDADGR
platenol.   LASTRTLFEH RAVVPCGGRG ELVAALGGFA AGRVSGGVRS GR..A.VPGG
monensin    LATTRAPLAH RAVLLGGDTA ELLGSLDALA EGAETASIVR GEAYT..EGR
oleandom    LATRRQVFER HAVVTGHDRE DLLNGLRDLE NGLPAPQVLL GRTPTPEPGG
tylosin     MAD.RSRFGY RAVVLARGEA ELAGRLRALA GGDPDAGVVT G...AVLDGG

            601                                                        650
niddam...   LALLFTGQGA QHPGMGQELY TTDPHFAAAL DEVCEELQRC GTQNLREVMF
platenol.   VGVLFTGQGA QWVGMGRGLY AGGGVFAEVL DEVLSMVGEV DGRSLRDVMF
monensin    TAFLFSGQGA QRLGMGRELY AVFPVFADAL DEAFAALDVH LDRPLREIVL
oleandom    LAFLFSGQGS QQPGMGKRLH QVFPGFRDAL DEVCAELDTH LGRLL.....
tylosin     VVVGAAPGGA GAAGGAGAAG GAGGGGVVLV FPGQGTQWVG MGAGLLGSSE

            651                                                        700
niddam...   TPDQPD.... .......... .......... LLDRTEYTQP ALFALQTALY
platenol.   GDVDVDAGAG ADAGAGAGAG VGSGSGSVGG LLGRTEFAQP ALFALEVALF
monensin    GETDSGGNVS GENVIGEGA. ......DHQA LLDQTAYTQP ALFAIETSLY
oleandom    .GPEAGPPLR DVMFAERGT. ......AHSA LLSETHYTQA ALFALETALF
tylosin     VFAASMRECA RALSVHVGWD LLEVVSGGAG .LERVDVVQP VTWAVMVSLA

            701                                                  ↓     750
niddam...   RTLTARGTQA HLVLGHSVGE ITAAHIAGVL DLPDAARLIT ARAHVMGQLP
platenol.   RALEARGVEV SVVLGHSVGE VAAATVAGVL SLGDAVRLVV ARGGLMGGLP
monensin    RLAASFGLKP DYVLGHSVGE IAAAHVAGVL SLPDASALVA TRGRLMQAVR
oleandom    RLLVQWGLKP DHLAGHSVGE IAAAHAAGIL DLSDAAELVA TRGALMRSLP
tylosin     RYWQAMGVDV AAVVGHSQGE IAAATVAGAL SLEDAAAVVA LRAGLIGRYL
```

↑ Fig 4B

```
          751                                                       800
niddam... HG.GAMLSVQ AAEHDLDQLA HTHG..VEIA AVNGPTHCVL SGPRTALEET
platenol. VG.GGMWSVG ASESVVRGVV EGLGEWVSVA AVNGPRSVVL SGDVGVLESV
monensin  AP.GAMAAWQ ATADEAAEQL AGHERHVTVA AVNGPDSVVV SGDRATVDEL
oleandom  GG.GVMLSVQ APESEVAPLL LGREAHVGLA AVNGPDAVVV SGERGHVAAI
tylosin   AGRGAMAAVP LPAGEVEAGL .AKWPGVEVA AVNGPASTVV SGDRRAVAGY

          801                                                       850
niddam... AQHLREQNVR HTWLKVSHAF HSALMDPMLG AFRDTLNTLN Y..QPPTIPL
platenol. VASLMGDGVE YRRLDVSHGF HSVLMEPVLG EFRGVVESLE FGRVRPGVVV
monensin  TAAWRGRGRK AHHLKVSHAF HSPHMDPILD ELRAVAAGLT FHE..PVIPV
oleandom  EQILRDRGRK SRYLRVSHAF HSPLMEPVLE EFAEAVAGLT FRA..PTTPL
tylosin   VAVCQAEGVQ ARLIPVDYAS HSRHVEDLKG ELERVLSGI. .RPRSPRVPV

          851                                                       900
niddam... ISNLTGQIA. .....DPNHL CTPDYWIDHA RHTVRFADAV QTAHHQGTTT
platenol. VSGVSGGVV. .....GSGEL GDPGYWVRHA REAVRFADGV GVVRGLGVGT
monensin  VSNVTGELVT ATATGSGAGQ ADPEYWARHA REPVRFLSGV RGLCERGVTT
oleandom  VSNLTG.... ..APVDDRTM ATPAYWVRHV REAVRFGDGI RALGKLGTGS
tylosin   CSTVAGEQPG EPVF...... .DAGYWFRNL RNRVEFSAVV GGLLEEGHRR

          901                                                       950
niddam... YLEIGPHPTL TTLLHHTL.. .DNP..... .........T TIPTLHRERP
platenol. LVEVGPHGVL TGMAGECLGA GDDV..... .........V VVPAMRRGRA
monensin  FVELGPDAPL SAMARDCFPA P......... .ADRSRPRPA AIATCRRGRD
oleandom  FLEVGPDGVL TAMARACVTA APEPGHRGEQ GADADAHTAL LLPALRRGRD
tylosin   FIEVSAHPVL V......... .....HAIEQ TAEAADRSVH ATGTLRRQDD

          951
niddam... EPETLTQAIA AVGVRTDGID WAVLCGASRP RRVELPTYAF
platenol. EREVFEAALA TVFTRDAGLD ATALHTGSTG RRIDLPTTPF
monensin  EVATFLRSLA QAYVRGADVD FTRAYGATAT RRFPLPTYPF
oleandom  EARSLTEAVA RLHLHGVPMD WTSVLGGDVS .RVPLPTYAF
tylosin   SPHRLLTSTA EAWAHGATLT WDPAL..PPG HLTTLPTYPF
```

niddam: niddamycin; platenol: platenolide I (spiramycin); oleandom: oleandomycin.

Fig 4c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+
6 methylmalonyl-CoA
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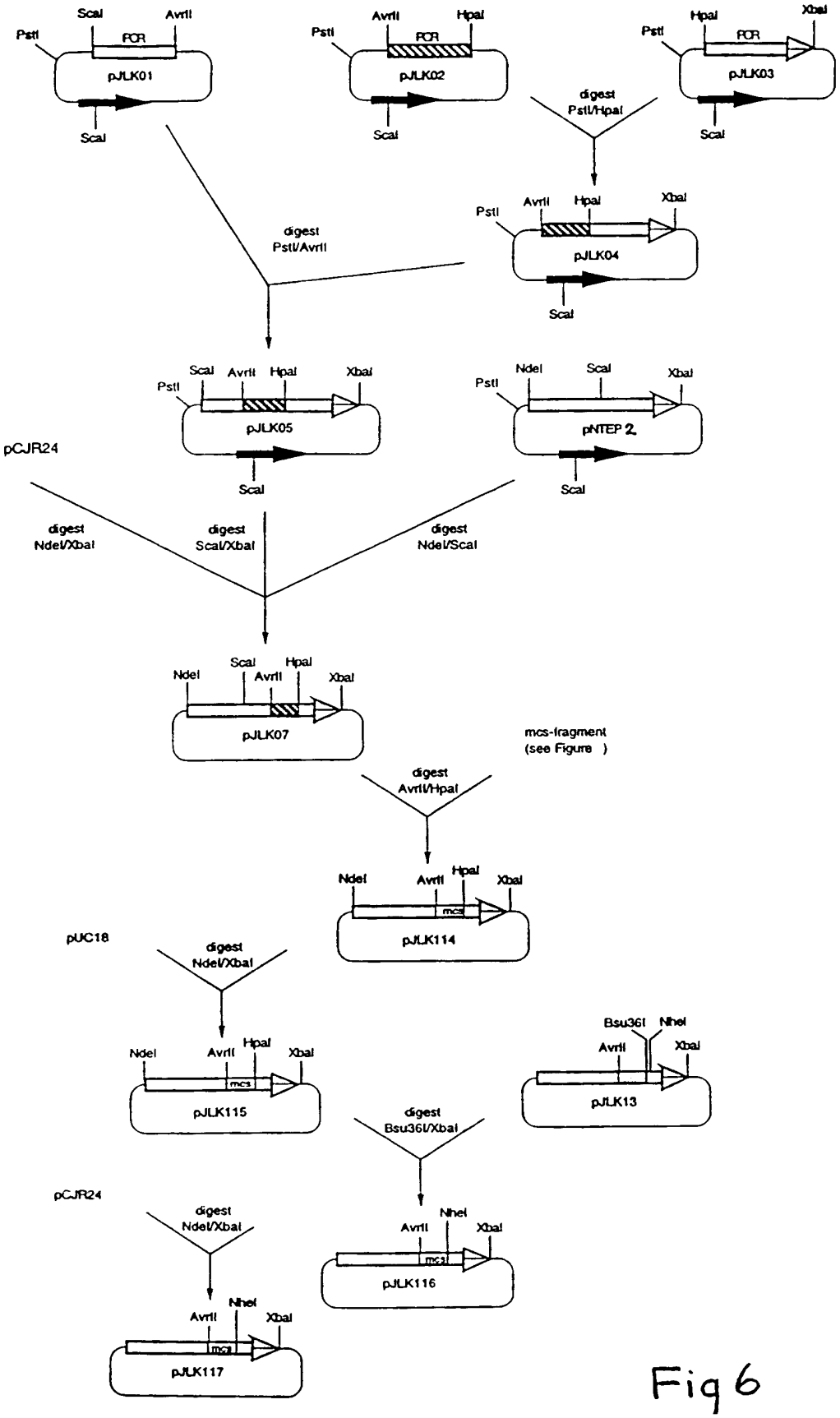
deoxyerythronolide B
eryF
erythronolide B
eryB
eryC
erythromycin D
eryK
erythromycin C
eryG
erythromycin A
desosamine
mycarose
cladinose

Fig. 5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HpaI
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pJLK02
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PstI
PCR
pJLK03
ScaI
digest
PstI/HpaI
PstI
AvrII
HpaI
XbaI
pJLK04
ScaI
digest
PstI/AvrII
ScaI
AvrII
HpaI
XbaI
PstI
pJLK05
ScaI
pCJR24
NdeI
ScaI
XbaI
PstI
pNTEP 2
ScaI
digest
NdeI/XbaI
digest
ScaI/XbaI
digest
NdeI/ScaI
NdeI
ScaI
AvrII
HpaI
XbaI
pJLK07
mcs-fragment
(see Figure)
digest
AvrII/HpaI
NdeI
AvrII
HpaI
XbaI
mcs
pJLK114
pUC18
digest
NdeI/XbaI
NdeI
AvrII
HpaI
XbaI
mcs
pJLK115
Bsu36I
NheI
AvrII
XbaI
pJLK13
digest
Bsu36I/XbaI
pCJR24
digest
NdeI/XbaI
AvrII
NheI
XbaI
mcs
pJLK116
NheI
AvrII
XbaI
mcs
pJLK117

Fig 6

Figure 7

forward (Plf):

5'-CTA GGC CGG GCC GGA CTG GTA GAT CTG CCT ACG TAT CCT TTC CAG GGC AAG CGG TTC TGG CTG CAG CCG GAC CGC ACT AGT CCT CGT GAC GAG

GGA GAT GCA TCG AGC CTG AGG GAC CGG TT-3'

backward (Plb):

5'-AAC CGG TCC CTC AGG CTC GAT GCA TCT CCC TCG TCA CGA GGA CTA GTG CGG TCC GGC TGC AGC CAG AAC CGC TTG CCC TGG AAA GGA TAC GTA

GGC AGA TCT ACC AGT CCG GCC CGG C-3'

oligos annealed:

```
CTAGGCCGGGCCGGACTGGTAGATCTGCCTACGTATCCTTTCCAGGGCAAGCGGTTCTGGCTGCAGCCGGACCGCACTAGTCCTCGTGACGAGGGAGATGCATCGAGCCTGAGGGACCGGTT
    CGGCCCGGCCTGACCATCTAGACGGATGCATAGGAAAGGTCCCGTTCGCCAAGACCGACGTCGGCCTGGCGTGATCAGGAGCACTGCTCCCTCTACGTAGCTCGGACTCCCTGGCCAA
-----               ------  ------                          ------        ------              ------    -------     ---
AvrII               BglII   SnaBI                           PstI          SpeI                NsiI      Bsu36I      HpaI
```